## REMARKS

The detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented in the foregoing section above, with an appropriate defined status identifier for each claim.

Claims 3-7, 9-14, and 16-27 are cancelled herein. The cancellation of claims does not constitute acquiescence in the propriety of any rejections set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the cancelled claims in subsequence divisional applications.

Claims 1, 8, and 15 are amended herein.

Newly added claims 28 and 29 are presented herein. Upon entry of the amendments herein, claims 1, 2, 8, 15, 28, and 29 are pending in this application.

The claim amendments herein do not contain new matter. The amendment to claims 1, 8, and 15 clarifies what Applicants regard as the invention. The amendment to claim 1 reciting "a polypeptide fragment comprising at least 30 contiguous amino acids" is supported throughout the specification, including at page 12, lines 21-24 ("a **fragment**... may be **at least** 5, 10, 15, 20, 25, **30**, 40, 50, 60, 75, 100, 150, 250 or at least 500 **contiguous** nucleotides or **amino acid residues** in length" [emphasis added in bold]).

Newly added claim 28, drawn to methods for screening a compound for effectiveness as an agonist of invention polypeptides, is supported throughout the specification, including at page 7, lines 1-8 ("the invention also provides a **method for screening a compound for effectiveness as an agonist** of a polypeptide... the method comprises a) exposing a sample comprising the polypeptide to a compounds, and b) detecting agonist activity in the sample" [emphasis added in bold]).

Newly added claim 29 is supported throughout the specification, including at page 7, lines 13-20 ("the invention also provides a **method for screening a compound for effectiveness as an antagonist** of a polypeptide... the method comprises a) exposing a sample comprising the polypeptide to a compounds, and b) detecting antagonist activity in the sample" [emphasis added in bold]).

The amendments herein to the specification do not contain new matter. As required by the Examiner, the amendment to the specification excises references to a hyperlink [Official Action, Item 11 at page 8, paragraph 2]. In response to the Examiner's requirement for a new title [Official Action, Item 12 at page 8, paragraph 3], the title is amended herein to recite "HUMAN ZINC FINGER RELATED PROTEINS".

For the reasons provided above, the amendments to the claims and specification do not contain new matter. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the arguments that follow.

**ARGUMENTS**

*Specification/ Informalities*

As required by the Examiner, the amendment to the specification excises references to a hyperlink [Official Action, Item 11 at page 8, paragraph 2]. In response to the Examiner's requirement for a new title [Official Action, Item 12 at page 8, paragraph 3], the title is amended herein to recite "HUMAN ZINC FINGER RELATED PROTEINS".

*35 U.S.C. §112, second paragraph*

In light of the claim amendments herein canceling claim 16, the Patent Office's rejection of claim 16 for alleged indefiniteness is rendered moot.

*35 U.S.C. §101 and §112, first paragraph- Utility*

Claims 1, 2, 8, 15, and 19 are rejected under 35 U.S.C. §101 and §112, first paragraph for alleged lack of a specific, substantial, or well-established utility. Specifically, the Patent Office alleges that "the specification fails to provide a specific benefit in currently available form" [Official Action, Item 14 at page 11, paragraph 2].

As amended herein, independent claim 1 is presently drawn to polypeptides comprising the amino acid sequence of SEQ ID NO: 19, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19, and polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO: 19. Dependent claim 15 is drawn to compositions comprising polypeptides of the claimed invention. Dependent claim 8 is drawn to methods for producing invention polypeptides and newly added dependent claims 28 and 29 are drawn to methods for screening a compound for effectiveness as an agonist and antagonist, respectively, of invention polypeptides.

**A. The Specification Provides Sufficient Guidance Regarding Therapeutic Indications for Use of Claimed Polypeptides**

The Patent Office alleges that "the specification fails to provide any guidance regarding those specific diseases- if any- that can be diagnosed, prevented, or treated" [Official Action, Item 14 at page 10, paragraph 1]. As a first point, the presently claimed invention does not pertain to methods of diagnosis, treatment, or prevention of reproductive, immune, neurological, and cell proliferative disorders. Nonetheless, Applicants respectfully assert that the specification does provide sufficient guidance regarding specific diseases which can be diagnosed, treated, or prevented with the claimed polypeptides.

The specification states that "expression of NuABP is closely associated with proliferative, neuronal, inflammed, and cancerous tissues and tissues of the reproductive system" and thus, "appears to play a role in reproductive, immune, and neurological disorders, and cell proliferative disorders" [Specification at page 30, lines 16-19]. Representative diseases associated with decreased expression or activity of NuABP are explicitly recited in the specification at page 30, lines 25- page 31, line 34. Therefore, contrary to the Examiner's allegation, the specification does explicitly recite specific disease which may be treated or prevented with invention polypeptides.

**B. The Specification Provides Sufficient Guidance Regarding Methods of Therapeutic Use of the Claimed Polypeptides**

The Patent Office alleges that the use of the claimed polypeptides in the diagnosis, treatment, and prevention of reproductive, immune, neurological, and cell proliferative disorders "are not substantial... due to the failure of the specification to provide necessary guidance for using the claimed polypeptide" [Official Action, Item 14 at page 10, paragraph 1]. Specifically, the Patent Office alleges that the specification does not provide "specific guidance as to how one would specifically treat such a disease, e.g. **route of administration** and **dosage**" [emphasis added in bold, Official Action, Item 14 at page 10, paragraph 1].

As a first point, the presently claimed invention does not pertain to methods of diagnosis, treatment, or prevention of reproductive, immune, neurological, and cell proliferative disorders. Nonetheless, Applicants respectfully assert that the specification does provide sufficient guidance on how one of ordinary skill may use invention polypeptides in the diagnosis, treatment, or prevention of reproductive, immune, neurological, and cell proliferative disorders. Moreover, the specification provides explicit guidance regarding routes of administration and dosages of the claimed polypeptides in such uses.

Contrary to the Patent Office's allegation, the specification does provide sufficient guidance regarding *administration* of the claimed polypeptides, such as "oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means" [Specification at page 37, lines 2-5]. For example, the specification provides guidance on suitable preparations for oral administration, such as tablets, dragee cores, or push-fit capsules [Specification at page 37, lines 15-17]. The specification also discusses suitable carriers, auxiliaries, excipients, disintegrating or solubilizing agents, coatings, dyestuffs or pigments, fillers or binders, and suitable liquids that can be admixed with invention polypeptides in oral pharmaceutical preparations [Specification at page 37, lines 13-34]. Additionally, the specification provides guidance on suitable preparations for parenteral administration, such as aqueous or oily solutions [Specification at page 37, lines 35- page 38, line 9]. The specification also discusses compatible buffers, viscosity changing substances, lipophilic solvents, non-lipid polycationic amino polymers, and stabilizers that can be formulated with invention polypeptides in parenteral preparations [Specification at page 38, lines 1-9]. Furthermore, the specification provides guidance on suitable preparations for nasal or topical administration, such as the inclusion of known penetrants in such formulations [Specification at page 38, lines 10-11].

Contrary to the Patent Office's allegation, the specification does provide sufficient guidance regarding *dosage* of invention polypeptides in pharmaceutical compositions. Therapeutically effective doses are described as the amount "which ameliorates the symptoms or

condition" and can be determined "by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the $ED_{50}$" [Specification at page 38, line 32- page 39, line 8].

Therefore, as evidenced, in part, by the exemplary citations discussed above, the specification does provide explicit guidance regarding routes of administration and dosages of invention polypeptides in the diagnosis, treatment, or prevention of various disorders, such as reproductive, immune, neurological, and cell proliferative disorders.

**C. The Specification Provides Guidance Regarding Use of the Claimed Polypeptides in Methods of Screening Compounds**

As provided by amendment herein, claims 28 and 29 are drawn to methods for screening a compound for effectiveness as an agonist and antagonist, respectively, of invention polypeptides. Applicants respectfully assert that the specification provides sufficient guidance regarding the use of the claimed polypeptides for such screening methods.

For example, the specification describes drug screening techniques where the claimed polypeptides "may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly" and "formation of binding complexes between NuABP and the agent being tested may be measured" [Specification at page 44, lines 22-26]. The specification also describes high throughput screening of compounds where "large numbers of different small test compounds are synthesized on a solid substrate" and "the test compounds are reacted with NuABP, or fragments thereof, and washed" [Specification at page 44, lines 27-31] prior to detection of bound NuABP. The specification further describes coating the claimed polypeptides onto plates for use in drug screening techniques [Specification at page 44, lines 31-32].

Therefore, as evidenced, in part, by the exemplary citations discussed above, the specification provides sufficient guidance regarding the use of the claimed polypeptides for methods of screening a compound for effectiveness as an agonist and antagonist.

*35 U.S.C. §112, first paragraph- Written Description*

Claims 1, 8, 15, and 16 are rejected under 35 U.S.C. §112, first paragraph for alleged lack of written description. Specifically, the Patent Office alleges that the "claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" [Official Action, Item 16 at page 12, paragraph 1].

**A. The Specification Describes Representative Species of the Claimed Genus**

The Patent Office alleges that "the disclosure of the single representative species is insufficient to be representative of the attributes and features of all species encompassed by the claimed genus" [Official Action, Item 16 at page 13, paragraph 1].

First, Applicants respectfully disagree with the Patent Office's allegation that "the specification discloses only a single representative species of the claimed genus of polypeptides, i.e. SEQ ID NO: 19" [Official Action, Item 16 at page 13, paragraph 1]. In addition to polypeptides comprising the amino acid sequence of SEQ ID NO: 19, the specification also describes, for example, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19 [Specification at page 5, lines 5-7] and polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO: 19 [Specification at page 15, lines 20-26]. The specification also provides exemplary methods of determining percent identity between polypeptide sequences, such as MEGALIGN version 3.12e sequence align program, CLUSTAL V, and BLAST2 version 2.0.9 [Specification at page 15, lines 4-19]. Therefore, the specification describes the complete chemical structure, *i.e.* SEQ ID NO: 19, for representative species of invention polypeptides and exemplary methods by which one of ordinary skill could make invention polypeptides.

Applicants also respectfully disagree with the Patent Office's allegation that "the genus of claimed polypeptides encompass species that are WIDELY variant in their structures and

functions" [Official Action, Item 16 at page 13, paragraph 1]. The presently claimed invention is drawn to polypeptides comprising the amino acid sequence of SEQ ID NO: 19, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19, and polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO: 19. Species of the claimed genus of polypeptides share chemical similarities, *i.e.*, SEQ ID NO: 19 and 90% sequence identity to SEQ ID NO: 19. In addition, species of the claimed genus of polypeptides share functional similarities, *i.e.*, polypeptides of the claimed invention are human nucleic-acid binding proteins. Therefore, species of the claimed genus of polypeptide share chemical as well as functional properties.

Because the claimed genus of polypeptides share similar chemical and functional properties and because the specification describes the chemical structure of a representative number of polypeptide species, Applicants respectfully assert that the specification describes distinguishing attributes and features of all polypeptides of the claimed invention.

The Patent Office further alleges that the specification "fails to provides those characteristics that distinguish "naturally occurring" polypeptides" [Official Action, Item 16 at page 14, paragraph 1] over non-naturally occurring polypeptides. In light of the claim amendments provided herein excising recitation of "naturally occurring" polypeptides, this allegation is rendered moot.

*35 U.S.C. § 112, first paragraph- Scope of Enablement*

Claims 1, 8, 15, and 16 are rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. The Patent Office admits that the specification is "enabling for the polypeptide of SEQ ID NO: 19" [Official Action, Item 17 at page 14, paragraph 2]; however, the Patent Office alleges that the "specification does not reasonably provide enablement for the broad scope of the claimed polypeptides, including all polypeptides comprising a naturally occurring amino acid sequence that is at least 90% identical to SEQ ID NO: 19" [Official Action,

Item 17 at page 14, paragraph 2]. As a first point, the claims have been amended herein excising recitation of "naturally occurring" polypeptides.

**A. Making and Using the Full Scope of Claimed Polypeptides is within the Scope of Routine for the Ordinary Artisan**

The Patent Office alleges that "undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed compound" [Official Action, Item 17 at page 14, paragraph 3]. Applicants respectfully disagree with the Patent Office's allegations and specifically refute the Patent Office's interpretations of the *Wands* factors in the present case.

**1. The Claimed Invention is Commensurate with the Disclosure of the Specification**

The present claims are commensurate in scope with the enabling disclosure provided by the present specification. Contrary to the Patent Office's allegation that the "disclosure is limited to... SEQ ID NO: 19" [Official Action, Item 17 at page 15, paragraph 1], the specification also describes, for example, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19 [Specification at page 5, lines 5-7] and polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO: 19 [Specification at page 15, lines 20-26]. Therefore, the specification describes the chemical structure, *i.e.* SEQ ID NO: 19, for a representative number of species of invention polypeptides.

**2. The Specification Provides Guidance on How to Make and Use the Invention**

The specification provides the necessary guidance to enable one of skill to make and use the entire scope of claimed polypeptides. Contrary to the Patent Office's allegation that the "specification fails to provide guidance for isolating all polypeptides encompassed by the scope of the claim" [Official Action, Item 17 at page 15, paragraph 2], the specification provides numerous exemplary techniques for isolation of invention polypeptides, including, but not limited to,

- recovery of cells transformed with polynucleotides encoding polypeptides of the claimed invention [Specification at page 27, lines 18- page 28, line 6],
- high performance liquid chromatography [Specification at page 25, lines 12-16],
- protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies [Specification at page 28, lines 17-18], and
- ligation of invention polypeptides to heterologous sequences, such as glutathione S-transferase, maltose binding protein, thioredoxin, calmodulin binding protein, and hemaglutin, to facilitate purification with commercially available affinity matrices [Specification at page 29, lines 25-33].

The Patent Office also alleges that the specification "fails to provide guidance for using those naturally occurring variants of SEQ ID NO: 19 that have a distinct biological activity" [Official Action, Item 17 at page 15, paragraph 2]. The specification provides guidance for numerous applications for invention polypeptides, including, for example, use of invention polypeptides for methods for screening a compound for effectiveness as an agonist or antagonist [Specification at page 44, lines 22-26 and at page 44, lines 27-32], and use of invention polypeptides in the diagnosis, treatment, or prevention of reproductive, immune, neurological, and cell proliferative disorders [Specification at page 30, lines 24-35]. Therefore, the specification enables one of skill to make and use the full scope of claimed polypeptides, as evidenced, in part, by the exemplary citations provided above.

**3. Claimed Polypeptides Share Functional Similarities**

The Patent Office alleges that "even if one were to succeed in isolating a variant using a SEQ ID NO:19- specific antibody, it is highly unpredictable as to whether the isolated variant will exhibit the same activity as SEQ ID NO:19" [Official Action, Item 17 at page 16, paragraph 1]. As a first point, the presently amended claims do not recite "immunogenic fragments" of

SEQ ID NO: 19. Additionally, as discussed above, the specification provides numerous exemplary methods for isolating invention polypeptides in addition to methods involving the use of SEQ ID NO: 19- specific antibodies.

Polypeptides of the claimed invention share functional similarities, *i.e.*, human nucleic acid binding proteins, and identification of invention polypeptides is not only predictable, it is within the scope of routine experimentation. Moreover, the specification provides sufficient guidance to enable one of skill in the art to perform such routine identification techniques. For example, the specification describes measuring the ability of invention polypeptides to stimulate transcription of the LacZ reporter gene in a $LexA_{op}$-LacZ gene construct [Specification at page 52, lines 18-28]. This assay method involves cloning inventive polynucleotides into a plasmid to encode for a LexA fusion protein, introducing this fusion construct and the $LexA_{op}$-LacZ construct in yeast cells, and assessing the amount of LacZ enzyme activity associated with the transformed cells, which is indicative of the amount of transcription stimulated by the tested invention polypeptide.

An additional exemplary method provided in the specification for measuring the ability of invention polypeptides to stimulate transcription involves monitoring expression of a marker protein, such as CD64 or CD64-GFP, in mammalian cells that have been co-transfected with inventive polynucleotides and plasmids encoding said marker protein [Specification at page 52, line 30- page 53, line 23]. In this assay, the influence of invention polypeptides on gene expression can be determined by measuring the amount of CD64 or CD64-GFP expressed on the surface of transfected cells.

Therefore, as evidenced, in part, by the exemplary citations discussed above, the specification provides sufficient guidance to enable one of skill in the art to identify invention polypeptides which function as human nucleic acid binding proteins.

**4. The State of the Art Demonstrates that Making and Using Invention Polypeptides is Within the Scope of Routine Experimentation**

The Patent Office alleges that the state of the art "provides evidence for the high level of unpredictability for isolating variants of SEQ ID NO: 19 using a SEQ ID NO: 19-specific antibody" [Official Action, Item 17 at page 16, paragraph 2]. As noted above, the present claims do not recite the phrase "immunogenic fragments" and the specification provides numerous methods for isolating invention polypeptides in addition to methods which involve SEQ ID NO: 19- specific antibodies.

Applicants respectfully disagree with the Patent Office's allegations and assert that isolation of invention polypeptides, all of which share chemical similarities, *i.e.*, relation to SEQ ID NO: 19, is predictable and well within the scope of routine experimentation for one of skill in the art. As discussed above in this Response, the specification provides exemplary techniques for isolation of invention polypeptides, including, but not limited to,

- recovery of cells transformed with polynucleotides encoding polypeptides of the claimed invention [Specification at page 27, lines 18- page 28, line 6],
- high performance liquid chromatography [Specification at page 25, lines 12-16],
- protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies [Specification at page 28, lines 17-18], and
- ligation of invention polypeptides to heterologous sequences, such as glutathione S-transferase, maltose binding protein, thioredoxin, calmodulin binding protein, and hemagluttin, to facilitate purification with commercially available affinity matrices [Specification at page 29, lines 25-33].

Therefore, as evidenced, in part, by the exemplary citations discussed above, isolation of invention polypeptides is predictable and within the scope of routine experimentation for one of skill in the art.

**5. The Amount of Experimentation Performed by the Ordinary Artisan is Routine**

The Patent Office alleges that "it is not routine in the art to screen for all polypeptides having a substantial number of substitutions or modifications and having *any* function, as encompassed by the instant claims" [Official Action, Item 17 at page 16, paragraph 3].

As a first point, contrary to the Patent Office's allegation, polypeptides of the claimed invention have a specific function, *i.e.*, human nucleic-acid binding proteins. Secondly, despite the labor-intensive nature of screening a large number of polypeptides, such well-known methods for identifying the claimed polypeptides is within the scope of routine experimentation for the skilled artisan. "The test [of undue experimentation] is not merely quantitative, sine a considerable amount of experimentation is permissible, if it is merely routine. ..." [*In re Wands*, 858 F.2d 731; MPEP 2164.06]. Moreover, as discussed above in this Response, the specification provides sufficient guidance to enable one of skill in the art to identify invention polypeptides which function as human nucleic acid binding proteins.

Therefore, Applicants respectfully assert that the amount of experimentation performed by one of skill in making and using invention polypeptides is within the realm of routine experimentation.

*35 U.S.C. § 102-Anticipation*

Claims 1 and 15 are rejected under 35 U.S.C. §102 for alleged anticipation by Sigma Chemical Company 1993 Catalog. Specifically, the Patent Office asserts that Sigma Chemical Company 1993 Catalog "teaches a biologically active fragment of SEQ ID NO:19, i.e., a glycylglutamine dipeptide" [Official Action, Item 18 at page 17, paragraph 3]. The claims have been amended herein and are drawn, in part, to isolated polypeptides comprising the amino acid sequence of SEQ ID NO: 19, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19, and polypeptide fragments comprising at least 30 contiguous amino

acids of SEQ ID NO: 19. Therefore, in light of the amendments herein excising recitation of "biologically active fragment", the rejection is rendered moot.

*35 U.S.C. § 103-Obviousness*

Claim 8 is rejected under 35 U.S.C. §103(a) for allegedly being unpatentable over Sigma Chemical 1993 Catalog in view of Parish et al. (Nature, Vol. 306: 267-270 (1983)). The Patent Office asserts that Sigma Chemical Company 1993 Catalog "teaches a biologically active fragment of SEQ ID NO:19, i.e., a glycylglutamine dipeptide" and the Patent Office further asserts that "Parish et al. teach isolation of a glycylglutamine dipeptide from porcine pituitary" [Official Action, Item 19 at page 18, paragraph 5]. The claims have been amended herein and are drawn, in part, to isolated polypeptides comprising the amino acid sequence of SEQ ID NO: 19, polypeptides comprising a sequence having at least 90% sequence identity to SEQ ID NO: 19, and polypeptide fragments comprising at least 30 contiguous amino acids of SEQ ID NO: 19. Therefore, in light of the amendments herein excising recitation of "biologically active fragments", the rejection is rendered moot.

## CONCLUSION

In light of the amendments and arguments provided herein, Applicants believe that the present application is now in condition for allowance. Entry of the claims as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date August 3, 2004

By 

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